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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,954	02/15/2002	Akira Kaji	K0448/7012	3440

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
06/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/980,954	KAJI ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 52-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 52-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1 and 52-59 are pending in the application.

[2] Applicant's amendment to the claims, filed on 3/26/07, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicant's amendment to the specification, filed on 3/26/07, is acknowledged.

[4] Applicant's arguments filed on 3/26/07 have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

Specification/Informalities

[6] The specification is objected to as being inconsistent in referring to Table 8 as being the structure coordinates of the RRF of SEQ ID NO:1 (see instant specification amendment). The first amino acid listed in Table 8 is a Val residue (see p. 64, top of the instant specification), while the first amino acid of SEQ ID NO:1 (according to the sequence listing filed on 12/4/01) is a Met residue. Clarification and/or appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

[7] Claims 1 and 52-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the conserved active site of RRF protein." There is insufficient antecedent basis for this limitation in the claim. Also, claims 52-59 recite the limitation "the active site of the RRF protein" and it is unclear as to whether this phrase refers to "the *conserved* active site of RRF protein" or is meant to encompass RRF conserved and non-conserved active sites. In the interest of advancing prosecution, the examiner has interpreted claims 52-59 as referring to the "conserved active site of RRF" as recited in claim 1. It is suggested that applicant clarify the meaning of the claims.

Claim Rejections - 35 USC § 112, First Paragraph

[8] Claims 1 and 52-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

MPEP § 2163.II.A.3.(b) states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or

amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description."

Claim 1 (claims 52-59 dependent therefrom) has been amended to recite, "employing a three-dimensional structure of the conserved active site of RRF protein, which protein binds ribosomal RNA and recycles ribosomes...wherein the conserved active site comprises Arginine at positions 110, 129, and 132 according to Table 8." At p. 5, top of the instant remarks, applicant points to pp. 11, 17, 21, 48, and original claim 1 as showing support for the added limitations. After reviewing applicant's cited disclosure, the examiner can find descriptive support for Arg110, Arg129, and Arg132 being the active site residues of SEQ ID NO:1 (see, *e.g.,* p. 11, lines 15-17). However, the examiner can find no support for the use of a 3-D structure of the "*conserved* active site of RRF," can find no support for Arg110, Arg 129, and Arg132 being a *conserved* active site of *any* RRF protein, *i.e.,* proteins other than SEQ ID NO:1, and can find no support for the function of an RRF protein as binding ribosomal RNA and recycles ribosomes.

Applicant is invited to show support the noted limitation(s).

[9] The written description rejection of claims 1 and 52-59 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant disagrees with the examiner's assertion that the claims broadly encompass the use of structural coordinates representing

homology models of an RRF protein. Applicant argues the claims have been amended to recite the structural coordinates are of the conserved active site of functional RRF protein, which protein binds ribosomal RNA and recycles ribosomes, wherein the conserved active site comprises Arg at positions 110, 129, and 132 according to Table 8. According to applicant, one of skill in the art would recognize that applicant invented the use of this conserved active site 3-D structure.

Applicant's argument is not found persuasive. The examiner maintains the position that the specification fails to adequately describe all members of the genus of RRF proteins and 3-D structures and corresponding structural coordinates thereof as encompassed by the claims. Contrary to applicant's position, the claims still broadly, but reasonably encompass the use of a 3-D structure of any RRF protein, including homology models that comprise Arg at positions 110, 129, and 132, which encompasses full-length RRF proteins. As noted in the prior Office action, MPEP 2111.01 states, "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." In construing the claims, it is noted that, while claim 1 recites the use of a 3-D structure of "the conserved active site of RRF protein...", the claim does not exclude any other additional amino acids being present in the 3-D structure, particularly as the claim recites, "wherein the conserved active site *comprises* Arginine..." (emphasis added), wherein the transitional phrase "comprises" is "inclusive or open-ended and does not exclude additional, unrecited elements" according to MPEP 2111.03. Thus, the claims encompass the use of any "RRF" protein, defined in the specification as "an RRF protein having an enzyme activity in an ordinary state" (p.

13, middle), which includes Arg at positions 110, 129, and 132. Also, it is noted that the recitation of "Arginine at positions 110, 129, and 132 according to Table 8" in claim 1 has been interpreted as only identifying the amino acids at positions 110, 129, and 132 of the 3-D structure of the "RRF protein" as being Arg, and not requiring that the 3-D structure *have the structural coordinates* of Arg110, Arg 129, and Arg132 of Table 8.

Accordingly, in view of a broad, but reasonable interpretation of the claims, the genus of 3-D structures and corresponding structural coordinates encompass homology models. The Court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single species

of the genus of 3-D structures as encompassed by the claims, *i.e.,* the 3-D structure of RRF having the structural coordinates of Table 8 and only a single species of RRF proteins, *i.e.,* SEQ ID NO:1. The specification fails to disclose any other species of 3-D structures of RRF proteins as encompassed by the genus, which encompasses species having widely variant structures. The structures of the genus are widely variant, encompassing the use of any 3-D structure of an "RRF protein", as long as the "RRF protein" comprises Arg at positions 110, 129, and 132. In this case, it is highly unpredictable as to whether the resulting homology model(s) will maintain a conformation of a biologically active RRF polypeptide, that is able to maintain the functions of binding ribosomal RNA and recycling ribosomes, which is evidenced by Flower ("Drug Design, Cutting Edge Approaches," Royal Society of Chemistry, Cambridge, UK, 2002), which, addressing the use of homology models for identifying lead drugs, discloses "[p]roblems still exist, however: the fitting together of protein domains in a multi-domain protein, the determination of the most likely conformation of protein loops, the correct positioning of amino acid side chains, flexible ligand docking - to name only a few" (p. 25, middle). According to MPEP § 2163.II.2.(a).ii), "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." As such, the single disclosed species of 3-D structures and corresponding structural coordinates is insufficient to be representative of the attributes and features of the genus of "RRF protein" 3-D structures as encompassed by the claims.

Thus, at least for the reasons of record and the reasons stated above, a skilled artisan would recognize that applicant was not in possession of all "RRF protein" 3-D structures and corresponding structural coordinates as encompassed by the claims. Given the lack of description of a representative number of species, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[10] The scope of enablement rejection of claims 1 and 52-59 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues "the claims now recite what the Examiner has acknowledged to be enabling." Applicant argues the claims are limited to requiring the 3-D structure of the conserved active site comprise Arg at positions 110, 129, and 132 according to Table 8, and that the RRF from which the structural information is drawn to have the recited functions of binding ribosomal RNA and recycling ribosomes. According to applicant, "the claims do not cover the use of homology models or other variants of RRF."

Applicant's argument is not found persuasive. The examiner maintains the position that the specification fails to fully enable all RRF proteins and 3-D structures and corresponding structural coordinates thereof as encompassed by the claims without requiring undue experimentation. Contrary to applicant's position, the claims still

broadly, but reasonably encompass the use of a 3-D structure of any RRF protein, including homology models, that comprise Arg at positions 110, 129, and 132. As noted in the prior Office action, MPEP 2111.01 states, "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." In construing the claims, it is noted that, while claim 1 recites the use of a 3-D structure of "the conserved active site of RRF protein...", the claim does not exclude any other amino acids being present in the 3-D structure, particularly as the claim recites, "wherein the conserved active site *comprises* Arginine..." (emphasis added), wherein the transitional phrase "comprises" is "inclusive or open-ended and does not exclude additional, unrecited elements" according to MPEP 2111.03. Thus, the claims encompass the use of any "RRF protein", defined in the specification as "an RRF protein having an enzyme activity in an ordinary state" (p. 13, middle), which includes Arg at positions 110, 129, and 132, which encompasses full-length RRF proteins. Also, it is noted that the recitation of "Arginine at positions 110, 129, and 132 according to Table 8" in claim 1 has been interpreted as only identifying the amino acids at positions 110, 129, and 132 of the 3-D structure of the "RRF protein" as being Arg, and not requiring that the 3-D structure *have the structural coordinates* of Arg110, Arg 129, and Arg132 of Table 8.

Accordingly, in view of a broad, but reasonable interpretation of the claims, the genus of 3-D structures and corresponding structural coordinates encompass homology models. The scope of the claims is not commensurate in scope with the enablement provided by the specification, particularly with respect to the recited 3-D structures and RRF proteins. Contrary to applicant's position, the claims are not so limited to that which

the examiner has acknowledged as being enabled by the instant specification, *i.e.,* the specification is enabling only for a method for using the 3-D structure of RRF having the structural coordinates of Table 8 and the RRF protein of SEQ ID NO:1.

As noted in the prior Office action, at the time of the invention, methods of using a 3-D structure of a polypeptide and generating homology models were known in the prior art. However, while methods of generating homology models of a protein using a set of structure coordinates was known, Lambert et al. (US Patent Application Publication 2004/013751; cited in a prior Office action) acknowledges that "[p]otential or existent homology models cannot provide the necessary degree of specificity" in the in silico design of modulators (p. 3, ¶[0017]). See also the teachings of Flower (*supra*) as noted above. Further, it was well-known in the prior art that polypeptides having disparate functions could share similar 3-D structures. For example, Hegyi et al. [*J Mol Biol* (1999) 288:147-164; cited in a prior Office action] teaches that an isomerase, an oxidoreductase, a hydrolase, and a lyase all share the same TIM-barrel fold (p. 148, left column, and Figure 1). Similarly, while methods of altering the amino acid sequence of a protein were known at the time of the invention, the effects of such alteration(s) were highly unpredictable. Thus, a skilled artisan would have recognized that there was a high level of unpredictability in using altered 3-D protein structures and altered proteins themselves as encompassed by the claims with an expectation that the altered 3-D structures and proteins represent a biologically relevant conformation of RRF.

The specification discloses only a single working example of a 3-D protein structure, *i.e.,* a 3-D structure of RRF having the structure coordinates of Table 8 and

only a single working example of an RRF protein, *i.e.*, the RRF protein of SEQ ID NO:1. The specification fails to disclose any other 3-D structures of RRF protein variants as encompassed by the claims and further fails to provide guidance for altering SEQ ID NO:1 or the 3-D structure of RRF having the structural coordinates of Table 8 with an expectation of maintaining the ability to bind ribosomal RNA and recycle ribosomes.

While methods of altering a protein or 3-D structure thereof were known at the time of the invention, it was not routine in the art to create a substantial number of altered proteins and 3-D structures thereof as encompassed by the claims without guidance as to which of those structures is useful according to the disclosed utility.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

[11] The rejection of claim(s) 1 and 52-59 under 35 U.S.C. 103(a) as being unpatentable over Wilson et al. (US Patent 5,856,116; cited in the IDS filed 2/18/2005; cited in a prior Office action) in view of Kaji et al. (*Biochem Biophys Res Comm* 250:1-4, 1998; cited in a prior Office action) and In re Gulack 217 USPQ 401 (Fed. Cir. 1983) is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues the structural coordinates of Table 8 are not non-functional descriptive material, because the coordinates represent an actual 3-D protein structure, which can be used with or without a computer to design binding compounds. According to applicant, without the structural coordinates, such a 3-D structure could not be produced.

Applicant's argument is not found persuasive. Contrary to applicant's position, the structural coordinate data of Table 8 are "descriptive material." The issue is whether or not the descriptive material is functional or non-functional. Applicant appears to take the position that the Table 8 data is functional as representing the 3-D structure of an actual protein. However, what the data represent does not appear to distinguish between functional and non-functional descriptive material. Instead, according to MPEP 2106, whether data is functional or non-functional is made based on a determination of whether the data imparts functionality when employed as a computer component. In this case, the RRF structural coordinate data of Table 8 are for processing – using a computer and a known algorithm – to transform the data into a 3-D structure. The data

are non-functional descriptive material because the data have no functional relationship with a computer that processes the data. In this case, there is no evidence of record that the data of Table 8 functionally affect the processing steps of the computer. For example, there is no evidence that the data of Table 8 interact with other computer hardware or software to affect the efficiency or accuracy or any other characteristic of computer processing. Rather the data of Table 8 appear to be used merely as input for a computer program that generates a three-dimensional structure of an RRF polypeptide. In other words, the data recited in claim 1 do not affect how a computer performs or functions. While applicant appears to take the position that generating a 3-D structure using the coordinate data of Table 8 does not require the use of a computer, the claims do not exclude the use of a computer for processing the data of Table 8, which are non-functional descriptive material, using a known algorithm. In this case, the data of Table 8 does not distinguish over the prior art of record, particularly as there is no evidence of record that the data can impart functionality.

Applicant argues the coordinate data are analogous to the elucidation of the structure of a chemical compound, with all the knowledge necessary to visualize the structure of RRF, including the active site, to allow for design or selection of binding compounds.

Applicant's argument is not found persuasive. In this case, the claims are not drawn to the use of a *polypeptide* having a particular structural formula, *i.e.,* amino acid sequence. Instead, the claims are drawn to the use of a 3-D model, an abstract representation of a protein. According to the specification (*e.g.,* beginning at p. 28,

middle), the 3-D model is generated using a computer, which processes the data of Table 8 using a known algorithm. Thus, the question is whether or not the data of Table 8 are functional or non-functional descriptive material and at least for the reasons of record and the reasons stated above, it is the examiner's position that the data of Table 8 are non-functional descriptive material.

Applicant argues the examiner's reliance on *In re Gulack* is inapplicable as a computer is not required to "draw the structure of the conserved active site of RRF proteins" and the structural coordinate data are "anything but merely descriptive; they represent the actual structure of a protein that was not previously available through teaching or suggestion." According to applicant, prior to the elucidation of the structure of the conserved active site of RRF, including Arg at positions 110, 129, and 132, no such 3-D structure could have been made in view of the combination of Wilson et al., Kaji et al., and using the legal precedent rationale of *In re Gulack*. Applicant argues that because the 3-D structure of RRF had not been previously recognized, one of ordinary skill in the art would have no reasonable expectation of success for practicing the claimed invention.

Applicant's argument is not found persuasive. As noted above, the claims are not drawn to the use of an actual protein, but to the use of a *3-D model* of an actual protein, based on the structural coordinates of Table 8. While applicant argues this 3-D model can be made without the use of a computer, in accordance with the specification, the claims nonetheless encompass the use of the structural coordinate data of Table 8 for processing by a computer using a known algorithm, *i.e.*, the claims do not exclude the

use of the structural coordinate data of Table 8 for processing by a computer using a known algorithm. The examiner acknowledges the prior art does not teach the 3-D structure of RRF nor the structural coordinates of Table 8. However, according to the Court's holding in *Gulack,* nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious. For reasons of record and those set forth above, it is the examiner's position that the Table 8 data is non-functional descriptive material and thus need not be taught by the prior art. Therefore, because the only limitation not taught by the prior art is the Table 8 data, which cannot distinguish the claimed invention over the prior art, one of ordinary skill in the art would have had a reasonable expectation of success for practicing the claimed invention and the claimed invention would have been obvious at the time of the invention using the legal precedent rationale of *In re Gulack*.

Conclusion

[12] Status of the claims:

Claims 1 and 52-59 are pending.

Claims 1 and 52-59 are rejected.

No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

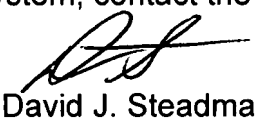
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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Art Unit 1656